Atrial Transport Function in Coronary Artery Disease: Relation to Left Ventricular Function

ROBERT I. HAMBY, MD, FACC, WILLIAM J. NOBLE, MD, FACC, DONALD H. MURPHY, PhD, IRWIN HOFFMAN, MD, FACC

Roslyn, New York

The atrial contribution to ventricular stroke volume was evaluated in 50 patients with coronary artery disease and found to be related to left ventricular function. All patients underwent complete hemodynamic and angiographic studies. Angiographic volume studies were utilized to determine atrial contribution to the stroke volume, end-systolic volume and ejection fraction. In 11 patients without heart disease, atrial contribution to stroke volume was (mean value ± standard deviation) 9.3 ± 6 ml/m² compared with 13.5 ± 6 ml/m² in the patients with coronary disease (probability [p] < 0.05). The percent of atrial contribution to stroke volume was 20 ± 7 and 33 ± 11%, respectively, in normal subjects and patients with coronary disease (p < 0.05). The combination of congestive heart failure and cardiomegaly was the only clinical aspect associated with a significantly higher (p < 0.05) atrial contribution to stroke volume than that in the remaining patients with coronary disease (46 versus 31%). Relating the atrial contribution to stroke volume to the left ventricular end-diastolic pressure, stroke volume, end-systolic volume and ejection fraction revealed correlation coefficients of 0.30, −0.44, 0.56 and −0.64, respectively. No patient with a normal ejection fraction (> 0.50) had an atrial contribution greater than 40% of stroke volume. The ratio of peak left ventricular systolic pressure/end-systolic volume (mm Hg/ml) was 2.7 ± 1.5 in patients (n = 14) with an atrial contribution greater than 40% of stroke volume compared with 5.3 ± 3.4 in patients having an atrial contribution of 40% or less (p < 0.01). These findings indicate that atrial contribution to stroke volume is inversely related to left ventricular function.

Atrial transport function has been the topic of many previous studies (1–23). Investigations in animals (4,5,7,13,14) and human beings (1–3,6,8–12,15–19,23) have demonstrated that properly timed left atrial contraction plays an important role in augmenting ventricular filling and improving left ventricular function. Atrial contraction increases both left ventricular end-diastolic pressure and volume, thus increasing the force of left ventricular contraction by way of the Frank-Starling mechanism and maintaining a low mean atrial pressure (3,5,13,20). These changes in left ventricular function, resulting from atrial contraction, in turn cause increased cardiac output, stroke volume and stroke work.

Investigators (1,11,12,15,24–26) differ as to the significance of properly timed atrial contraction in patients with myocardial disease. The present report quantitatively defines the atrial contribution to forward stroke volume in a group of patients with coronary artery disease and varying left ventricular function. Such information may be highly relevant in clinical situations calling for permanent pacemaker implantation. Several studies (22,27–31) have shown that in some patients, the implantation of a right ventricular pacemaker may be followed by giddiness, dizziness, syncope and hypotension (pacemaker syndrome) attributed to reduced cardiac output secondary to loss of atrial function.

Methods

Study patients. Fifty patients referred for angina pectoris due to significant coronary artery disease proved by selective coronary arteriography form the basis of this report. These patients, 40 men and 10 women, had a mean age of 54 years (range, 39 to 74) and included 25 patients with triple vessel coronary disease and 12 and 13 having single and double vessel disease, respectively. All patients underwent comprehensive evaluation, including a complete history and physical examination, standard 12 lead electrocardiogram, posteroanterior and lateral chest X-ray films as well as a complete right and left heart catheterization with left ventricular angiography and selective coronary arteriography. All patients with complicating valvular heart disease were excluded as were patients whose left ventricular angiograms were not satisfactory for deter-

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Address for reprints: Robert I. Hamby, MD, The Heart Center, St. Francis Hospital, Roslyn, New York 11576.

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mining left ventricular volumes because of poor contrast cine films or instances of two consecutive beats preceded by a ventricular premature beat. Furthermore, patients were excluded if the various phases of filling during diastole could not be delineated (see later). This invariably necessitated eliminating patients who had a heart rate of 90 beats/min or greater during the time of the left ventricular angiogram. The electrocardiographic diagnosis of prior myocardial infarction was made on the basis of accepted criteria (32); the diagnosis of cardiomegaly from the chest X-ray film was made independently by a radiologist. Another 11 patients, without evidence of heart disease after such complete evaluation, were designated as the control group in the study.

Hemodynamic and angiographic studies. These studies were performed by methods and criteria previously published (33). Left ventricular cineangiograms were obtained in the right anterior oblique position after power injection of 0.5 to 0.75 ml/kg body weight of 76% sodium meglumine diatrizoate into the left ventricle over 2 to 3 seconds. During angiography, the electrocardiogram was monitored to rule out catheter-induced ventricular premature beats and to record the heart rate. The average heart rate during angiography was 66 beats/min (range, 50 to 86). A grid was positioned at the approximate location of the left ventricle and a short film strip was taken to permit correction due to magnification.

Left ventricular volumes were obtained by the area-length method (34,35). End-diastole was defined from the frame occurring immediately before the appearance of contrast medium above the aortic valve, whereas end-systole was the frame showing the minimal left ventricular area obtained by planimetry. Left ventricular filling was evaluated by determining consecutive volumes during diastole to identify diastasis and the augmentation of left ventricular filling occurring during atrial systole (Fig. 1). Diastasis (Fig. 1, small arrows) is readily defined when the heart rate is less than 90 beats/min (7,26). The change in left ventricular volume as a result of atrial systole was designated as atrial contribution and was calculated by subtracting the average volume of the last three frames of diastasis from the end-diastolic volume. The mean values ($\pm$ standard deviation of the mean) for left ventricular end-diastolic volume, stroke volume and ejection fraction determined in the patients with a normal left ventricle using the methods described were 69 $\pm$ 19 ml/m^2, 47 $\pm$ 14 ml/m^2 and 0.68 $\pm$ 0.10 ml/m^2, respectively. Peak left ventricular systolic pressure was divided by end-systolic volume to reflect an index of ventricular contractility (36,37).

Statistical analysis. The statistical inference establishing confidence levels in this study employs a small sample analysis in conjunction with Fisher's *t* table. The correlation coefficients were determined by linear multiple regression analysis.

Results

Atrial contribution to stroke volume. The volume of blood delivered to the left ventricle as a result of left atrial contraction (Fig. 1, Va) was 9.3 $\pm$ 6 and 13.5 $\pm$ 6 ml/m^2, respectively, in the control subjects (n = 11) and patients with coronary artery disease (n = 50; $p < 0.05$). The ratio of the volume delivered as a result of atrial contraction to the stroke volume, representing (when multiplied by 100) the percent of atrial contribution to stroke volume was 20 $\pm$ 7 and 33 $\pm$ 11%, respectively, in the control and coronary disease groups ($p < 0.05$). None of the control patients had an atrial contribution greater than 40% whereas in 14 (28%) of the patients with coronary disease atrial contraction contributed more than 40% to stroke volume.

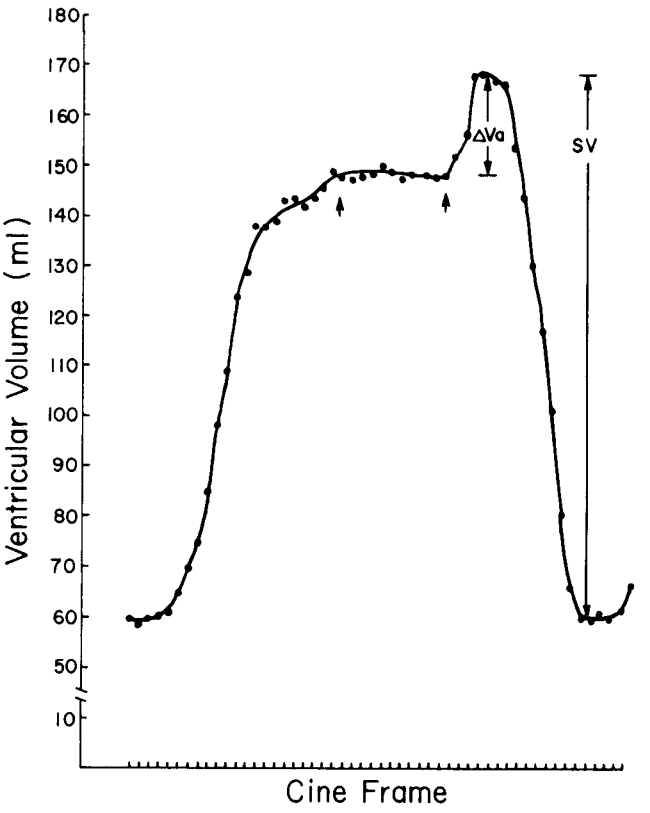

Figure 1. Left ventricular volume (ml) plotted for consecutive frames demonstrating phases of ventricular filling, with diastasis encompassing portion included between small **arrows.** Active phase of filling (ΔVa) and stroke volume (SV) are depicted.

Clinical factors affecting atrial contribution to stroke volume. The relation of the atrial contribution to stroke volume to various clinical features was reviewed. The presence or absence of a history of congestive heart failure (atrial contribution, 40 $\pm$ 11 and 30 $\pm$ 10%, respectively) or cardiomegaly (atrial contribution, 43 $\pm$ 10 and 32 $\pm$ 12% respectively) were not significant, although differences were noted. However, the combination of both congestive heart failure and cardiomegaly increased the mean atrial contribution to stroke volume to 46 $\pm$ 8%, a value greater ($p < 0.05$) than that noted (31 $\pm$ 11%) in patients without these two clinical features. Coronary group patients without electrocardiographic evidence of a prior infarction had an atrial contribution to stroke volume of 25 $\pm$ 8% that was lower but not significantly different from that of patients having inferior (32 $\pm$ 9%) or anterior (37 $\pm$ 14%) infarction. Two patients with multiple infarctions had an atrial contribution of 46 and 51%, respectively.

Relation to ventricular pressure and volume and ejection fraction. The relation of the atrial contribution to stroke volume to left ventricular end-diastolic pressure, stroke vol-

ume, end-systolic volume and ejection fraction is presented in Figures 2 to 5. The left ventricular end-diastolic pressures showed a weak correlation ($r = 0.30$) with the atrial contribution to stroke volume (Fig. 2). However, of the 14 patients with an atrial contribution greater than 40%, only 1 (7%) had an end-diastolic pressure less than 20 mm Hg. In contrast, of the 36 patients with an atrial contribution to stroke volume of 40% or less, 61% had an end-diastolic pressure less than 20 mm Hg ($p < 0.01$). The stroke volume showed a significantly inverse correlation ($p < 0.01$) to the atrial contribution to stroke volume ($y = -44$), indicating that the atrial contribution to stroke volume increases as forward stroke volume decreases (Fig. 3). Thus, of the 20 patients with a stroke volume less than 40 ml/m^2, 55% had an atrial contribution exceeding 40% compared with 3 (10%) of 30 patients with a stroke volume of 40 ml/m^2 or greater ($p < 0.005$).

The end-systolic volume had a significant ($p < 0.001$) direct relation ($r = 0.56$) to the atrial contribution to the stroke volume (Fig. 4). A significant inverse correlation ($r = -0.64$) was observed between the ejection fraction and the atrial contribution (Fig. 5.). No patient with a normal ejection fraction (≥ 0.5) had an atrial contribution greater than 40%. The ratio of peak left ventricular systolic pressure/end-systolic volume (mm Hg/ml) was 2.7 ± 1.5 in patients with an atrial contribution to stroke volume greater than 40% compared with 5.3 ± 3.4 in the remaining patients with coronary disease ($p < 0.01$).

Discussion

In our experience, atrial systole contributed 20% (range, 11 to 27) to forward stroke volume in patients without evidence of heart disease. In other studies (9,21,24,26) utilizing similar angiographic methods, atrial contribution to stroke volume ranged from 21 to 26%. In these cineangiographic studies, the ventricular volumes were determined in consecutive frames during diastole (Fig. 1) to define both the passive and active phases of ventricular filling. Passive ventricular filling consists of an early rapid increase in ventricular volume and is followed by diastasis. Diastasis is characterized by a marked reduction in the rate of filling that terminates (at heart rates less than 90 beats/min) with no change in ventricular volume (Fig. 1). In such circumstances, active ventricular filling as a consequence of atrial systole can be easily delineated by an abrupt increase in ventricular volume beginning 150 to 200 ms before end-diastole. At heart rates greater than 90, diastasis is shortened or lost in such a manner that rapid filling merges into active filling (7). Thus, angiographic methods necessitate utilizing clinical case material in studies performed at heart rates less than 90 to permit precise definition of the active phase of ventricular filling (26).

Previous studies using cardiac pacing techniques. Most clinical studies evaluating atrial function have utilized atrial, right ventricular or sequential atrioventricular pacing techniques, alone or in combination (1,2,6,8,10–12,15–19,23,32). In these studies, fixed right ventricular pacing was accompanied by a 10 to 50% decrease in stroke volume compared with atrial or atrioventricular pacing at similar heart rates. The wide range noted in the reduction in stroke volume as a result of right ventricular pacing may in part be related to the heart rate. In both dogs (4,7) and human subjects (12) the atrial contribution to stroke volume is related to heart rate. With increasing heart rate, a progressive increase in the atrial contribution to stroke volume occurs. Reiter and Hindman (12) found that stroke volume with sequential atrioventricular pacing at rates of 75, 85 and 100 beats/min was, respectively, 17, 23 and 29% greater than with fixed right ventricular pacing at similar rates.

Limitation of pacing technique. The comparison of data derived from studies utilizing angiographic methods with those reported after pacing faces major inherent limitations

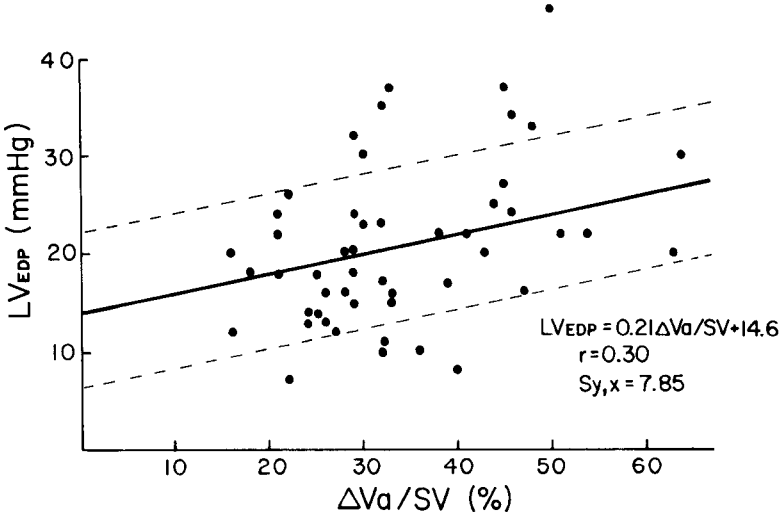

Figure 2. Relation between left ventricular end-diastolic pressure (LVEDP) and atrial contribution to stroke volume (ΔVa/SV). Shown are regression equation (**solid line**), correlation coefficient (r) and 1 standard error of the estimate (Sy,x) with the latter depicted by **dashed lines.**

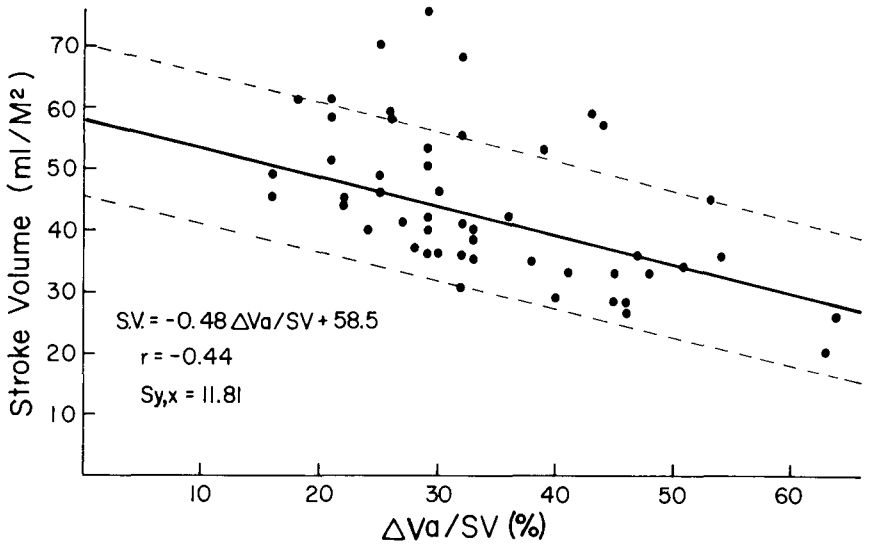

Figure 3. Relation between stroke volume (S.V.) and atrial contribution to stroke volume (ΔVa/SV). Shown are regression equation (**solid line**), correlation coefficient (r) and 1 standard error of the estimate (Sy,x) with the latter depicted by **dashed lines**.

based on methodology. Angiographic methodology simply derives the volume of blood delivered to the left ventricle as a result of atrial systole and relates that as a percent of the forward stroke volume. Pacing studies determine stroke volume changes presumably resulting from loss of a properly timed atrial contraction. However, pacing studies may alter variables that do not necessarily relate to the volume of blood delivered to the left ventricle, but that may, nevertheless, change the forward stroke volume. Thus, right ventricular pacing may alter the normal sequence of ventricular activation (38,39) and at times affect proper atrioventricular valve closure (4,33,40–42), both of which can, in a given instance, alter stroke volume. Finally, right ventricular pacing will decrease preload, resulting in variable reduction of left ventricular emptying depending on the resting state of the myocardium (3,4,13,20,33,42). Thus, the decrease in stroke volume during right ventricular pacing may be greater than that due to the simple elimination of the volume change resulting from atrial systole (33). The present study is directed only at evaluating the relation, if any, of left ventricular function in patients with coronary artery disease to the volume of blood delivered by left atrial systole—the latter expressed as the percent of forward stroke volume.

Role of left atrium in left ventricular function. Left atrial function can be conveniently divided into two phases. The first phase provides a storage reservoir of blood during ventricular systole and the second provides a conduit for the passage of blood from the pulmonary veins to the left

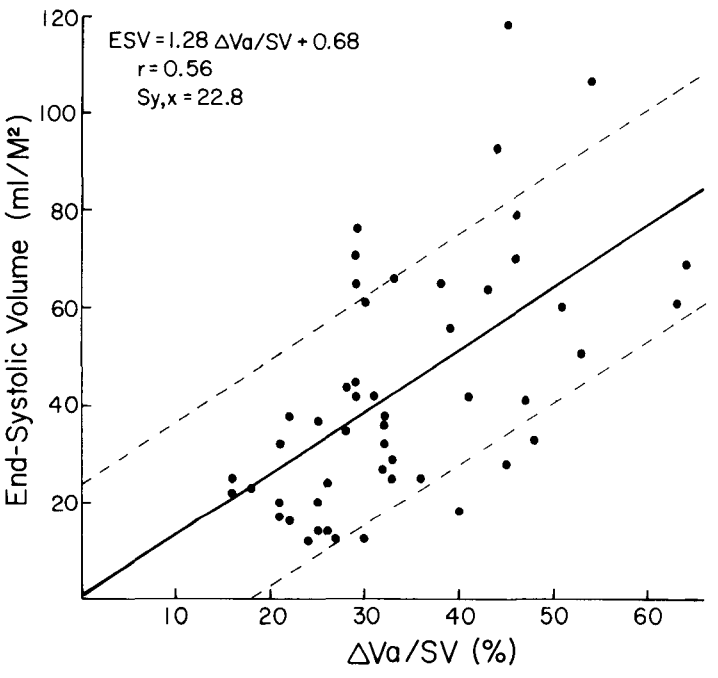

Figure 4. Relation between end-systolic volume (ESV) and atrial contribution to the stroke volume (ΔVa/SV). Shown are regression equation (**solid line**), correlation coefficient (r) and 1 standard error of the estimate (Sy,x) with the latter depicted by **dashed lines**.

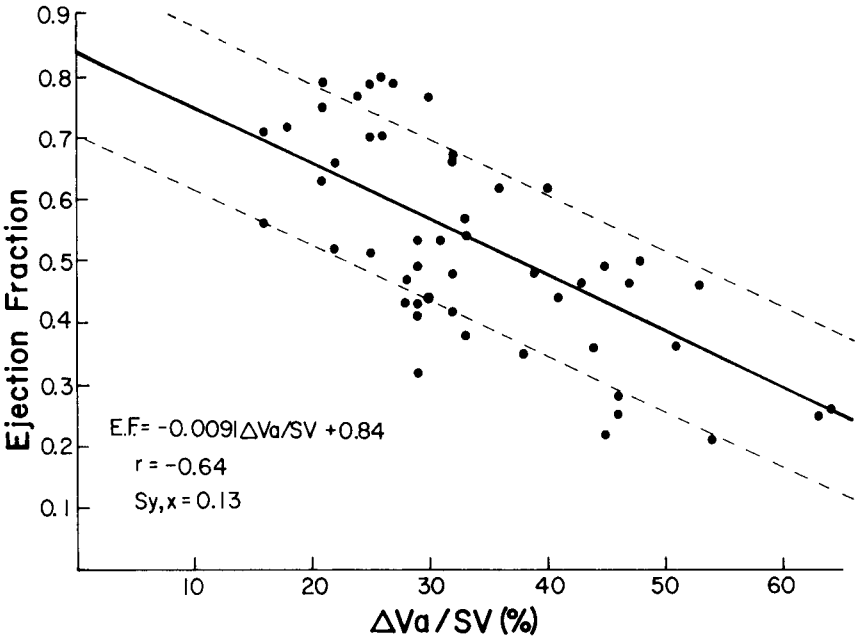

Figure 5. Relation between ejection fraction (E.F.) and atrial contribution to the stroke volume (ΔVa/SV). Shown are regression equation (**solid line**), correlation coefficient (r) and 1 standard error of the estimate (Sy,x) with the latter depicted by **dashed lines**.

ventricle during diastole (21). In the absence of mitral valve insufficiency, the volume of blood delivered as a result of left atrial storage and conduit function is equal to stroke volume. The conduit function of the left atrium can be divided into passive and active phases, with the latter related to left atrial contraction. This active filling of the left ventricle not only increases the volume of blood delivered, but can alter left ventricular contraction as a result of the Frank-Starling mechanism (3,13,20,42). The present study and others (7,21,24,26) indicate that passive filling of the left ventricle delivers approximately 80% of the forward stroke volume while active filling approximates 20%. Some studies (1,25,33) suggest that in the presence of myocardial disease, the loss of the active ventricular filling phase may be associated with deterioration of left ventricular function. In some pacing studies (22,27–31), right ventricular pacing was poorly tolerated and associated with lightheadedness, dizziness and hypotension, suggesting a critical decrease in cardiac output related to loss of active right atrial transport function. The present study indicates that the magnitude of the active phase of ventricular filling is indeed related to left ventricular function.

Role of coronary artery disease and ventricular dysfunction. Our patients with coronary artery disease, but no prior myocardial infarction, had an atrial contribution to stroke volume within the same range as that of patients without any heart disease (20 ± 7%) and none greater than 39%, similar to the experience reported by Bristow et al. (24). In contrast, Rahimtoola et al. (9), in 17 patients evaluated during the course of acute myocardial infarction, found a significant increase in atrial contribution to stroke volume compared with values in control subjects. Our patients with old anterior myocardial infarction tended to have a higher atrial contribution than did patients with inferior myocardial infarction (37 versus 32%), and in two patients with multiple infarctions almost 50% of the stroke volume was contributed by atrial contraction. A previous history of heart failure or the presence of cardiomegaly also was associated with an increased atrial contribution to stroke volume (40 and 43%, respectively), but the combination of both heart failure and cardiomegaly was the only clinical feature associated with a significantly ($p < 0.05$) higher atrial contribution to stroke volume (46 ± 8%) than that of the remaining patients. These limited observations are consistent with a relevant role of atrial contraction in the setting of clinical variables reflecting left ventricular dysfunction.

Correlation with hemodynamic findings and left ventricular function. The hemodynamic findings in our study corroborate the clinical impression that atrial contribution to forward stroke volume is related to underlying left ventricular function. The poor correlation ($r = 0.30$) between the left ventricular end-diastolic pressure and atrial contribution to stroke volume as noted (Fig. 2) probably reflects the effect of compliance on end-diastolic pressure. A similar finding was observed by Hammermeister and Warbasse (26). However, of the 23 patients with an end-diastolic pressure less than 20 mm Hg, only 1 (4%) had an atrial contribution greater than 40%; however, of the remaining 27 patients with a higher end-diastolic pressure (≥ 20 mm Hg), 48% had an atrial contribution to stroke volume greater than 40% ($p < 0.01$). Pacing studies, on the other hand, have indicated that pulmonary capillary wedge pressure has no relation to the incremental decrease in cardiac output associated with right ventricular pacing (12); also at higher filling pressures, atrial contraction is ineffective in augmenting stroke volume (15). The differences between these studies (12,15) and our

present observations probably reflect basic differences in methodology. The inverse relation between forward stroke volume and atrial contribution (Fig. 3) is in agreement with the study of Rahimtoola et al. (9) in patients with acute myocardial infarction. They observed that atrial contraction contributed 56% to the stroke volume in patients with a cardiac index of 2.0 liters/min per m^2 or less compared with 31% in patients with a higher cardiac index. Thus, we confirm that as the stroke volume decreases, the role of atrial contraction becomes of paramount importance.

Left ventricular function was evaluated utilizing three variables—end-systolic volume, ejection fraction and the peak left ventricular systolic pressure/end-systolic volume ratio. End-systolic volume and ejection fraction are interrelated and are both accepted as reflecting overall left ventricular pump function. There was a good correlation between atrial contribution to stroke volume and these two variables of left ventricular pump function, indicating a definite tendency for atrial contraction to contribute a greater percent to the stroke volume with increasing evidence of deterioration of global left ventricular function (Fig. 4 and 5); however, there is considerable spread along the regression line as indicated by the standard error of the estimate. If an atrial contribution greater than 40% reflects an increased atrial contribution to stroke volume, such patients have a significantly greater incidence ($p < 0.01$) of abnormal left ventricular pump function. Finally, utilizing the peak left ventricular systolic pressure/end-systolic volume ratio, a significantly lower index ($p < 0.01$) of contractility was found in those patients with an atrial contribution to the stroke volume exceeding 40% (2.7 ± 1.5 versus 5.3 ± 3.4).

Clinical implications. Our observations confirm previous reports (1,9,21) that left atrial contraction contributes a greater proportion to cardiac output in the presence of left ventricular dysfunction than in patients with normal left ventricular function. However, this conclusion does not take into consideration the atrial contribution to ventricular preload (33). A previous study (33) in patients with coronary artery disease has revealed that the loss of atrial contraction during right ventricular pacing will result in decreased preload that, by itself, may, in some patients, result in deterioration of left ventricular function. However, in such patients, left ventricular dysfunction preexisted. In clinical situations calling for a permanent pacemaker, the presence of left ventricular dysfunction (for example, radionuclide ejection fraction <0.5) suggests that a permanent atrioventricular sequential pacemaker will best preserve and maintain cardiac output.

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